

CLAIMS

1. A method of modulating cholesterol efflux in a cell, said method comprising
5 modulating expression and/or activity of sterol 27-hydroxylase (CYP27) and/or caveolin-1 or equivalent thereof in the cell.
2. A method according to claim 1 wherein the cell is selected from the group including hepatic cells or hepatocytes, macrophages, endothelial cells,
10 smooth muscle cells and other cells of the vessel wall and stem cells.
3. A method according to claim 2 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a cell deriving from a vessel wall associated with an atherosclerotic plaque.
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4. A method according to claim 2 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a vessel cell, smooth muscle cell or endothelial cell.
- 20 5. A method according to claim 2 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a macrophage.
6. A method according to claim 2 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a stem cell.
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7. A method according to claim 6 wherein the stem cell is a haematopoietic stem cell.
8. A method according to claim 2 wherein the expression and/or activity of
30 caveolin-1 is modulated in a hepatic cell or hepatocyte.
9. A method according to any one of claims 1 to 8 wherein the cholesterol effluxed is substantially non-oxidised cholesterol.

10. A method according to any one of claims 1 to 9 wherein the cell is transfected with an operably linked CYP27 and/or caveolin-1 gene or equivalent thereof to modulate expression and/or activity of CYP27 and/or caveolin-1 in the cell.

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11. A method according to any one of claims 1 to 10 wherein the cell is further treated with a demethylating agent.

12. A method according to claim 11 wherein the demethylating agent is 5-azacytidine.

13. A method of increasing cholesterol efflux in a cell, said method comprising
increasing expression and/or activity of sterol 27-hydroxylase (CYP27)
and/or caveolin-1 or equivalent thereof in the cell.

14. A method according to claim 13 wherein the expression of the gene encoding CYP27 and/or caveolin-1 or equivalent thereof is increased.

15. A method according to claim 13 or 14 wherein the activity of CYP27 and/or caveolin-1 or equivalent thereof is increased.

16. A method according to claim 13 wherein the cell is transfected with a gene encoding CYP27 and/or caveolin-1 or equivalent thereof and expression of the gene is increased to increase cholesterol efflux.

17. A method according to any one of claims 13 to 16 wherein the cell is further treated with a demethylating agent.

18. A method according to claim 17 wherein the demethylating agent is 5-azacytidine.

19. A method according to any one of claims 14 to 18 wherein the gene is induced to increase expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof.
- 5 20. A method according to anyone of claims 13 to 19 wherein the cell is selected from the group including hepatic cells or hepatocytes, macrophages, endothelial cells, smooth muscle cells and other cells of the vessel wall and stem cells.
- 10 21. A method according to claim 20 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a cell deriving from a vessel wall associated with an atherosclerotic plaque.
22. A method according to claim 21 wherein the expression and/or activity of
15 CYP27 and/or caveolin-1 or equivalent thereof is modulated in a vessel cell, smooth muscle cell or endothelial cell.
23. A method according to claim 20 wherein the cell is a macrophage.
- 20 24. A method according to claim 20 wherein the expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof is modulated in a stem cell.
25. A method according to claim 24 wherein the stem cell is a haematopoietic stem cell.
- 25 26. A method according to claim 20 wherein the expression and/or activity of caveolin-1 is modulated in a hepatic cell or hepatocyte.
27. A method according to any one of claims 13 to 26 wherein the
30 cholesterol effluxed is substantially non-oxidised cholesterol.
28. A cell having modulated cholesterol efflux, said cell comprising modulated expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof.

29. A cell according to claim 28 wherein the cell is transfected with a gene encoding CYP27 and/or caveolin-1 or equivalent thereof.
- 5 30. A cell according to claim 28 or 29 selected from the group including hepatic cells or hepatocytes, macrophages, endothelial cells, smooth muscle cells, cells of the vessel wall and stem cells.
31. A cell according to claim 30 which is a hepatic cell.
- 10 32. A cell according to claim 30 which is a stem cell.
33. A cell according to claim 32 wherein the stem cell is a haemotopoietic stem cell.
- 15 34. A cell according to any one of claims 28 to 33 having increased cholesterol efflux, said cell comprising increased expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof.
- 20 35. A method of treating a cholesterol related condition in a patient by modulating cholesterol efflux from a cell of the patient, said method comprising:
modulating expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof in the cell.
- 25 36. A method of treating a cholesterol related condition in a patient according to claim 35 by modulating cholesterol efflux in a cell in the patient, said method comprising:
introducing a gene construct to modulate expression and/or activity of CYP27 and/or caveolin-1 or equivalent in the cell of the patient.
- 30 37. A method according to claim 36 wherein the gene construct includes a gene encoding CYP27 and/or a CYP27 regulator and/or caveolin-1 and/or a caveolin-1 regulator.

38. A method according to any one of claims 35 to 37 wherein the expression and/or activity of CYP27 and/or caveolin-1 is increased.

39. A method of treating a cholesterol related condition in a patient by
5 modulating cholesterol efflux in the patient, said method comprising:
introducing a modulated cell to the patient, wherein said cell comprises
modulated expression and/or activity of CYP27 and/or caveolin-1 or equivalent
thereof.

10 40. A method according to claim 39 wherein the modulated cell is transfected
with a gene encoding CYP27 and/or caveolin-1 or equivalent thereof.

41. A method according to claim 39 or 40 wherein the expression and/or
activity of CYP27 and/or caveolin-1 or equivalent thereof in the modulated cells
15 is increased.

42. A method according to any one of claims 34 to 40 wherein the cells are
selected from the group including hepatic cells or hepatocytes, macrophages,
endothelial cells, smooth muscle cells and other cells of the vessel wall and
20 stem cells.

43. A method according to any one of claims 42 wherein the cell is a hepatic
cell.

25 44. A method according to claim 42 wherein the cell is a stem cell.

45. A method according to claim 44 wherein the cell is a haematopoietic
stem cell.

30 46. A method according to claim 42 wherein the cell is a macrophage.

47. A method according to claim 42 wherein the cell is a vessel cell,
endothelial cell or a smooth muscle cell.

48. A method according to any one of claims 39 to 47 wherein the cells are introduced into a region of disease associated with cholesterol accumulation.
49. A method according to claim 48 wherein the cells are introduced to vessel cells which line the vessel.
50. A method according to any one of claims 39 to 49 wherein the cholesterol related condition is selected from the group including myocardial infarction, atherosclerosis, stroke, hypoalphalipoproteinaemia or peripheral vascular disease.
51. A method according to claim 50 wherein the cholesterol related condition is atherosclerosis.
52. A method of identifying a compound which modulates cholesterol efflux in a cell, said method comprising:
contacting the compound to the cell;
detecting a change in expression and/or activity of CYP27 and/or caveolin-1 or equivalent thereof in the cell relative to a cell which has not been contacted with the compound.
53. A method according to claim 52 wherein the cell is selected from the group including endothelial cells, smooth muscle cells and vessel cells, hepatic cells or hepatocytes, macrophages, and stem cells.
54. A method according to claim 53 wherein the cell is a hepatocyte.
55. A method according to claim 54 wherein the cell is a hepatocyte transfected with caveolin-1.
56. A method according to claim 54 or 55 wherein the cell is a HepG2 cell.
57. A composition when used for treating a cholesterol related condition, said composition comprising:

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a compound in an amount effective to treat the condition wherein said compound is identified by the method according to any one of claims 52 to 56; and

admixing the compound.

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58. A method according to claim 1 substantially as hereinbefore described with reference to the examples and/or figures.